REMARKS

The present Amendment is being submitted in response to the Office Action mailed June 5, 2009. Claims 1-70 have been canceled without prejudice. Claims 71-84 are pending in the present application.

On page 4 of the Office Action the Examiner rejected claims 55, 62 and 71 under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner rejected the claims because they refer to specific figures of the patent application. The Examiner relies upon MPEP§ 2173.05(s) and *Ex Parte Fressola*, 27 USPQ2d, 1608, 1609 (Bd. Pat. App; & Inter. 1993) to support this rejection. Applicants have reviewed MPEP § 2173.05 (s) and *Ex Parte Fressola* and do not agree with the Examiner's interpretation of these materials and do not agree with the Examiner's rejection under 35 U.S.C. § 112. However, in an effort to expedite prosecution, Applicants have canceled claims 55 and 62 without prejudice and have amended claim 71 to delete the reference to Figure 6. Based upon the present amendments, Applicants submit the rejection under 35 U.S.C. § 112 is moot.

On pages 4-7 of the Office Action the Examiner rejected claims 55-78 under 35 U.S.C. § 103(a) as being unpatentable over, Mehta et al., United States Patent No. 5,837,284 ("Mehta") in view of Mulye, United States Patent No. 6,475,493 ("Mulye") and Beiman et al., United States Patent No., 6,312,728 ("Beiman").

In response to this rejection Applicants have amended the pending claims to recite a controlled release methylphenidate tablet consisting of three elements: 1) an immediate release methylphenidate layer; 2) a compressed methylphenidate tablet core comprising a hydrogel polymer

and methylphenidate and 3) an enteric coating surrounding the compressed core. The claims also require the claimed tablet to exhibit specific *in vitro* and *in vivo* properties. Claim 72 has also been amended to incorporate the limitations of canceled claim 63. New claims 79-84 recite specific embodiments of the present invention, specifically claims 79-80 and 82-83 require the enteric coating to comprise a mixture of zein and another enteric polymer as taught by the examples of the present application.

Applicants have also amended claims 71, 77 and 78 to indicate the compressed core may contain a lubricant.

No new matter is added by the present claims. Support can be found in the claims previously submitted and page 4, lines 2-20, page 7, lines 1-31, page 8, lines 5-22 and Examples 1-4 of the application as originally filed.

The present invention is a controlled release methylphenidate tablet that is easy to manufacture comprising an immediate release methylphenidate layer and a sustained release tablet core. The core is a compressed mixture of methylphenidate and a hydrogel polymer. This compressed mixture is coated with an enteric polymer, preferably a mixture of enteric polymers. Unlike any of the prior art references, the release of the methylphenidate from the core is controlled and sustained in part by the hydrogel polymer. This sustained release is confirmed by the recited *in vitro* dissolution parameters. The recited *in vitro* parameters require testing in an aqueous medium with a pH of 7.5. This pH is basic and is a pH where most enteric polymers readily dissolve. The sustained release of methylphenidate in a basic media is not disclosed or suggested by the prior art.

Mehta teaches a pulsatile dosage form comprising controlled release pellets wherein the coating on the pellets controls the release of the methylphenidate. Mehta does not teach or suggest

a single compressed tablet core surrounded by a single enteric coating. The Examiner admits that Mehta does not disclose enteric coatings or the core materials recited in the pending claims. In addition to these deficiencies, Mehta fails to disclose the sustained *in vitro* parameters recited in the pending claims. Mehta's pulsatile delivery system is designed to provide an immediate release dose of methylphenidate with 15-30 minutes after ingestion and a second burst or dose after a lag time. The second dose is delivered quickly, about 70-90% in about 0.5-2.5 hours preferably in about an hour. See Mehta, Col. 5, line 66 to Col. 6, line 17.

The tablet recited in the pending claims does not exhibit this rapid release of the second dose of methylphenidate. Rather, the tablet of the present invention requires a sustained release of the second dose of methylphenidate. In fact, Mehta teaches away from the present invention on Col. 2, lines 42-49 wherein it is stated that "sustained release formulations of methylphenidate have been shown to have lower efficacy than conventional dosage forms." This statement combined with the rapid release information of the second dose on Col. 5, line 66 to Col. 6, line 17 of Mehta would discourage a skilled artisan from preparing a hydrogel core that sustains the release of methylphenidate as recited in the present claims.

Mulye, like Mehta also teaches a multiparticulate or pelleted dosage system. Mulye requires the pellets to be coated with a coating comprising at least 75% of a water insoluble polymer and 1-25% of an enteric polymer. Mulye provides no motivation to modify the teachings of Mehta and thereby arrive at the present invention. In fact, the teachings of Mulye are similar to the teachings of Mehta in that the coated cores exhibit a quick release of drug after a specific time period. For example Col. 16, lines 45-60 of Mulye report the results of *in vitro* testing on dosage forms prepared according to Mulye. The data reports a slow release at low pH of about 1.2 - 4.5,

but a "rapid release in pH 7.4".

Therefore, the addition of Mulye to Mehta would not lead a skilled artisan to the present invention which requires a tablet that slowly releases the methylphenidate at a pH of 7.5. At best the addition of Mulye to Mehta would lead a skilled artisan to believe the coating of Mehta can be modified to include up to 30% of an enteric polymer. This amount of enteric polymer is substantially below the 45% required by the pending claims.

The addition of Beiman to Mehta and Mulye will not overcome the above identified deficiencies and lead a skilled artisan to the present invention. Beiman, like Mehta and Mulye, teaches a pelletized dosage form and not an enteric coated compressed hydrogel tablet as recited in the pending claims. More importantly, Beiman teaches coatings consisting essentially of enteric polymers that dissolve at a pH of 5.0 or higher. Beiman further teaches that the pellets are designed to be coated with multiple layers that will provide doses of the drug at specific pH environments along a patient's gastrointestinal tract. Beiman does not teach or disclose the possibility of a sustained release methylphenidate product as required by the pending claims.

If the enteric coatings of Beiman were employed on either the Mulye or Mehta pellets, the resulting pellets would rapidly release the methylphenidate from the core when tested in an aqueous media with a pH of 7.5 as recited in the pending claims.

Applicants submit that combining the disclosures in Mehta, Mulye and Beiman would lead a skilled artisan to a multi-particulate formulation with a coating that contains less than 30% enteric polymers and which provides a pulsatile release of methylphenidate and not a compressed hydrogel tablet that releases the methylphenidate in a sustained manner at high pHs.

On page 6 of the Office Action, the Examiner asserts "[i]f the prior art has the same

components, then the properties of the composition will necessarily follow." Applicants respectfully disagree with this overly broad statement. It is well recognized in the art that the release of a drug from a solid dosage form will depend upon many factors such as the solubility of the drug and excipients, the amount of the drug and excipients in the dosage form and the size and type of dosage form. For example, it is generally understood that varying the thickness of a polymer coating and composition of the polymer coating can affect the release rate of a drug from the dosage form. *See generally*: Mehta, Col. 10, lines 16-24. Similarly, it is also understood that dosage forms with large surface areas such as pellets have different release characteristics compared to dosage forms with smaller surface areas such as tablets because of the area exposed to the fluid environments. *See generally*: Beiman, Col. 1, line 66 to Col. 2, line 9.

A reference disclosing a specific component, without any guidance on the amounts, grade or manner in which it should be employed in a formulation, does not necessarily lead a skilled artisan to a create a specific dosage form with specific *in vitro* and *in vivo* parameters. Therefore, it is respectfully submitted that the Examiner's broad general statement regarding the properties of a composition will necessarily follow from the mere disclosure of components is not accurate and should not be a basis for rejecting the present claims.

Because the cited prior art references do not disclose or suggest an enteric coated methylphenidate tablet with a compressed hydrogel core that exhibits an *in vitro* sustained release of methylphenidate at a pH of 7.5, it is requested that the above 35 U.S.C. §103(a) rejection be withdrawn.

Based upon the above remarks and amendments, Applicants respectfully submit that claims 71-84 are allowable over the prior art and that the present application is in proper form for

allowance. Favorable consideration and early allowance is respectfully requested and earnestly solicited.

If the Examiner does not believe the pending claims are in the form for allowance, Applicants request that the Examiner contact the undersigned to schedule an in person or telephonic interview to discuss ways to further expedite prosecution of this application.

It is believed that no fee is required for the submission of the present amendment. The present Amendment is being filed within three (3) months of the mailing date of the non-final office action. The three (3) month date was Saturday June 5, 2009. The next business day after the Labor Day Federal Holiday is today, June 8, 2009. If a fee is due, the Commissioner is authorized to charge deposit account No. 08-1540.

Respectfully submitted,

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